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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/553,969	04/21/2000	Donald G. Wallace	17067-002040	6560

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/553,969	WALLACE ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,19-21 and 23-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,19-21,23-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment, remarks ad terminal disclaimer all dated 2-13-06 is acknowledged.

Terminal Disclaimer

The terminal disclaimer filed on 2-13-06 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US 6,063,061 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The following rejection of record has been maintained:

Claim Rejections - 35 USC § 102

1. Claims 1, 19-24, 28, 29 and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,110,484 to Sierra et al (Sierra).

Sierra discloses a biomedical implant comprising a matrix material and a biodegradable porosifying agent. Example 3 of Sierra (col. 7, lines 60 through col. 8, lines 1-20) disclose the preparation of cross-linked gelatin, in which gelatin is diluted with phosphate-buffered saline, cross-linked with SPEG, allowed to cool and form a gel. The resulting gel is lyophilized and pulverized (reads on instant fragmented) to particles of 20 to 150 microns. The resulting powdered gelatin is loaded into a syringe together with fibrinogen-Factor XII. Thus, the pulverized gelatin of Sierra meets the claim limitations fragmented, biocompatible, resorbable, single-phase aqueous colloid and the claimed particle size. With respect to the claim limitation "substantially free of free aqueous phase", the lyophilized and pulverized gelatin is essentially free of water. With

respect to the degradation rate, the limitation is inherent to the pulverized gelatin because Sierra teaches the preparation of gelatin in the same procedure as in the instant examples. Therefore, the reference anticipates instant claims.

2. Claims 1, 20-23, 25, 30 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,818,517 to Kwee et al (Kwee).

Kwee et al discloses a pharmaceutical preparation comprising a hydrogel polymer and a drug, which is introduced by means of an injection syringe, which reads on the instant applicator having an extrusion orifice. Kwee teaches that the composition provides water necessary for the preparation of the highly viscous hydrogel that is already part of the total composition (col. 1). Thus, the composition of Kwee does not contain any free aqueous phase other than the water that forms a part of the hydrogel. Kwee teaches that the polymer has a swelling capacity but does not state the claimed percentages. However, Kwee teaches dextrin as a suitable polymer (examples), which is a polysaccharide and thus the swelling capacity is inherent to dextrin of Kwee et al. Further, the claimed property of in vivo degradation time being less than one year is inherent to the polymer because Kwee teaches the same class of polymer i.e., a polysaccharide.

Claim Rejections - 35 USC § 103

3. Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,110,484 to Sierra.

Sierra, discussed above, fails to specify the addition of an active agent together with the resorbable colloid as claimed. However, Sierra suggests adding a number of active agents such as growth factors, clotting factors, antimicrobial etc., to the biodegradable polymer matrix (col. 4, lines 49-67 and example 4). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to add active agents such thrombin or other growth factors, antimicrobials etc., to the gelatin gel before loading the gel into the plunger of the syringe and delivering to the site of interest depending the required treatment in addition to wound healing or tissue remodeling because Sierra suggests matrix implants form dressings at the dressing or remodeling tissue site and yet enable release the desired therapeutic agents due to the fast in vivo degradation of the porosifying agents such as gelatin, calcium alginate etc.

4. Claims 19, 24, 31, 32 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwee et al (Kwee).

Instant claims are directed to protein and non-biological hydrogel and particle size of the hydrogel. While Kwee does not explicitly teach the claimed features, Kwee teaches a hydrogel polymer and suggests polymers such as dextran, starch, polyvinyl alcohol, etc (col. 2) are capable of swelling in water and homogenously injected out of the syringe without causing any practical problems and release the drug slowly over a period of time. Further, Kwee teaches that the polymer is in the form of dry particles (claims) and also suggests that the hydrogel can be used in combination with any drug

such as locally active drugs, bactericidal, anti-inflammatories, etc. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use a particulate natural or synthetic (non-biological) polymer such as polyvinyl alcohol, having an appropriate particle size, as a hydrogel in combination with the any desired drug because Kwee suggests that the dry particulate polymer which has a capability to swell is useful in releasing the drug over a long period of time without having the conventional drawbacks such as water being separated from the hydrogel during injection at the site of interest.

5. Claims 26-29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwee et al (Kwee) in view of Berg et al.

Kwee fails to teach the claimed protein polymer, a clotting agent such as thrombin, or the claimed combination of polymers.

Berg teaches a collagen wound dressing material comprising resorbable collagen particles of 50 to 350 microns. Berg also teaches addition of several wound-healing agents such as growth factors, enzyme inhibitors, angiogenesis factors etc (col. 4). Berg teaches that collagen would dressings are capable of swelling at the desired ratios and still be injectable (examples 5 and 10). Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ particulate collagen of Berg as a hydrogel in the teachings of Kwee and use the hydrogel alone or in combination with the hydrogels of Kwee for releasing drugs such as wound healing agents because Berg suggests that collagen dressings are capable of being resorbable,

allow cellular in growth, and protect the wound to be treated while still permitting the required diffusion of gases and liquids.

Response to Arguments

Applicant's arguments filed 2-13-06 have been fully considered but they are not persuasive.

Sierra- Claims 1, 19-24, 28, 29 and 34:

Applicants argue that Sierra describes a freeze-dried powder of gelatin-SPEG gel and not an aqueous colloid. Applicants further argue that in Example 3, Sierra discloses reconstituting the lyophilizate with Tris buffered saline to form slurry and not a fragmented single-phase aqueous colloid as presently claimed. It is argued that there is no teaching or suggestion that the resultant slurry when fully hydrated has a subunit size in the range from 0.01mm to 5mm, nor that the teaching or suggestion has an equilibrium swell from 400% to 5000%, nor that the resultant slurry has an in vivo degradation time of less than one year. Applicants also state that the gelatin of Sierra is prepared in a method that is different from that of instant gelatin (comparison table) and argue that there is no basis for inherency rejection because the claimed degradation time has not been shown to flow as a natural consequence from the technological constraints of Sierra. Applicants' arguments are not persuasive because instant specification fails to define a colloid and therefore can be given the broadest reasonable interpretation. Slurry by definition is a thin watery mixture of a fine insoluble material and a colloid is a dispersion of fine particles in a medium. Thus, slurry of Sierra by definition

is not different from a colloidal dispersion. Further, Sierra discloses that Tris buffered saline is forced into the diluent chamber to mix with the gelatin-fibrinogen mixture and thus, gelatin is not present as a dry powder and is instead mixed with the buffer that is aqueous in nature. Applicants' argument regarding the preparation of gelatin is not persuasive because, the lyophilized and pulverized gel of Sierra is further mixed with the aqueous Tris buffer and incubated for several minutes before use, which according to the described steps (in the comparison table of the remarks) is enough to form an aqueous colloid. Further, the arguments regarding the inherent properties are not persuasive because the process of preparation described by Sierra reads on the process steps described in the instant specification (page 24, lines 15-23) and hence possesses the same properties as claimed.

Applicants state that claims 19-21 are canceled. However, examiner notes that the claims are not canceled and are still pending.

Sierra-claims 25-29:

Applicants argue that Sierra fails to teach or suggest each and every element of claim 1 and therefore claims 25-29 that are directly dependent from claim 1 are allowable as depending from an allowable base claim. Applicants arguments are not persuasive because examiner explained the reasons for maintaining the rejection of claim 1 over Sierra also suggests adding a number of active agents such as growth factors, clotting factors, antimicrobial etc., to the biodegradable polymer matrix (col. 4, lines 49-67 and example 4). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to add active agents such

thrombin or other growth factors, antimicrobials etc., to the gelatin gel before loading the gel into the plunger of the syringe and delivering to the site of interest depending the required treatment in addition to wound healing or tissue remodeling because Sierra suggests matrix implants form dressings at the dressing or remodeling tissue site.

Kwee- claims 1, 20, 21, 23, 25, 30 and 35:

Applicants argue that Kwee describes a two-phase hydrogel that has a first phase including water-insoluble polymer and a second phase including a water-soluble thickening agent. It is argued that there is no teaching that the water-insoluble polymer, when swelled with water, would exist in a single phase along with the thickening agent or water-soluble thickener, when dissolved in water, would exist in a single phase along with the water-insoluble polymer. Therefore, it is argued that neither of the two phases of Kwee anticipates instant single-phase aqueous colloid, which is substantially free from a free aqueous phase.

Applicants' arguments are not found persuasive because, the disclosure of Kwee nowhere suggests that the hydrogel comprises two phases. Kwee teaches that the two-compartment syringe contains swellable polymer in one compartment and a thickening agent in either or both the compartments (lines bridging col. 1-2). Kwee teaches that the thickening (water-soluble) agent is added to absorb additional water that is left after the insoluble polymer is swelled. Thus, the insoluble polymer forms a hydrogel alone, without a need for the water-soluble thickener and hence the aqueous colloid is made of the swollen polymer alone. The water-soluble thickener is present only to absorb the remaining water and is very evident from the teachings of Kwee that the latter is not a

part of the swollen polymer. Further, applicants defines the term "hydrogel" (page 18, lines 7-11) as a composition "comprising" a single aqueous phase colloid and also describes the hydrogel as "comprises", thus allowing for the additional components such as thickening agents of Kwee to be present. Therefore, the rejection has been maintained.

Kwee: claims 19, 24, 31, 32 and 36:

Applicants argue that Kwee fails to teach or suggest all the limitations of claim 1 and for the same reasons; Kwee fails to teach the elements of instant claim 36. It is argued that claims 24, 31 and 32 are directly dependent from claim 1 and hence should be allowable for the above reasons. Applicants' arguments are not persuasive because as explained in the previous paragraph, Kwee discloses the claimed product. Further, with respect to the non-biological polymer of claim 36, Kwee suggests polyvinyl alcohol, dextrin and starch as equivalents for their suitability as a swelling polymer. Kwee also suggests adding drugs to composition comprising hydrogel for delivering to the site of application. Therefore it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use a particulate natural or synthetic (non-biological) polymer such as polyvinyl alcohol, having an appropriate particle size, as a hydrogel in combination with the any desired drug because Kwee suggests that the dry particulate polymer which has a capability to swell is useful in releasing the drug over a long period of time without having the conventional drawbacks such as water being separated from the hydrogel during injection at the site of interest.

Kwee in view of Berg:

Applicants argue that Kwee fails to teach or suggest each and every element of independent claims and that Berg fails to remedy the deficiencies of Kwee because Berg fails to disclose a single-phase aqueous colloid that is substantially free from a free aqueous phase. It is argued that Berg fails to teach the limitations of claim 1, claim 34 and also lacks suggestion for claims 26-29 and 33. It is to be noted that a rejection under this section is applicable to claims 26-29 and 33 but not 34. Applicants' arguments have been considered but not found persuasive because as explained in the previous paragraphs, Kwee does teach the claimed product. The motivation to add the collagen hydrogels of Berg to the composition of Kwee comes from the fact that both Kwee and Berg are directed to hydrogel polymers for therapeutic purposes and Berg suggests that collagen hydrogels are capable of swelling, injectable and are resorbable by the body. It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ particulate collagen of Berg as a hydrogel in the teachings of Kwee and use the hydrogel alone or in combination with the hydrogels of Kwee for releasing drugs such as wound healing agents because Berg suggests that collagen dressings are capable of being resorbable, allow cellular in growth, and protect the wound to be treated while still permitting the required diffusion of gases and liquids.

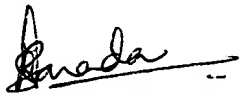
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala
Examiner
Art Unit 1615

April 25, 2006